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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	:	Kornelia Berghof et al.
Serial No.	:	10/691,731
For	:	NUCLEIC ACID MOLECULE SET FOR DETECTING SALMONELLA, NUCLEIC ACIDS, KIT AND USE
Filed	:	October 23, 2003
Examiner	:	Sitton, Jehanne Souaya
Art Unit	:	1634

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New York, NY 10151

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on.

Ronald R. Santucci, Reg. No. 28,988
(Name of Applicant, Assignee of Registered Representative)

Signature

September 9, 2008
Date of Signature

DECLARATION UNDER 37 C.F.R. §1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, Dr. Kornelia Berghof-Jaeger of Rhodelaenderweg 85, D-12355 Berlin, a citizen of Germany, hereby declare:

- that I have a degree in Biotechnology having studied at the Technical University in Berlin;

- that subsequent to my undergraduate degree, I worked as Scientist at the Oxford University in Great Britain from 1984-1986;

- that I received a Ph.D. in Biotechnology (Doktor Ingenieur) at the Technical University in Berlin in 1990, having worked at the Technical University in Berlin (Institute for Microbiology and Genetics) and the Oxford University (Department of Biochemistry);

- that I entered the employ of Biotecon GmbH in 1990, where I was appointed Managing Director and shareholder of the company and was responsible for the research and development of the company;

- that I subsequently became the Managing Director of Biotecon Diagnostics GmbH in 1998 and am responsible for the research and development department;

- that I am a member of numerous work and planning groups such as DIN (German Standardisation Organization), BGVV (German Foods and Health Authority), Dechema (German Association of Chemistry and Biotechnology);

- that I am the chairman of the working group "PCR for the detection of food borne pathogens in food" within CEN, the European Committee for Standardisation;

- that I have authored or co-authored 25 articles, including articles in the field of *Salmonella* detection, such as:

    - "Multicenter validation study of two blockcycler- and one capillary-based real-time PCR methods for the detection of *Salmonella* in milk powder," International Journal of Food Microbiology, 117(2):211-218 (June 2007).

I am the same Kornelia Berghof who is named as first inventor of U.S. Ser. No. 10/691,731 ("the '731 application"), filed on October 23, 2003. I am familiar with the invention described in the '731 application and am familiar with its prosecution history, in particular, the Office action mailed on April 16, 2008.

I understand that the Examiner withdrew rejections under 35 U.S.C. § 102(b) and 103(a) in view of amendments made to the claims. The Examiner acknowledged that neither Holmes (WO 95/00664) nor the prior art teaches or suggests constructing nucleic acid molecules with the specific sequence of SEQ ID NOS: 2, 4, 5, 7, 8, 10, or as presently claimed in the '731 application.

I further understand that the Examiner rejected all pending claims, claims 22, and 29-33[1] for allegedly entering new matter in claim 22 and for failing to comply with the written description requirement under 35 U.S.C. § 112, ¶1. Specifically, the Examiner's rejections assert that the claims are broader or contain subject matter that does not convey that the inventors, at

[1] The Supplemental Amendment—After Non-final Rejection filed on November 13, 2007 included two new claims numbered 30. For purposes of this declaration, I have assumed that the claim numbers will be corrected, and the pending claims are claims 22 and 29-33.

the time the application was filed, had possession of the claimed invention. The Examiner's assertions are incorrect, for the reasons more fully described below.

The pending amended claims reflected in the Supplemental Amendment—After Non-Final Rejection filed on November 13, 2007, now read as follows:

> 22. A set of isolated nucleic acid molecules comprising at least five isolated nucleic acid molecules selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and SEQ ID NO: 10 and the complementary sequence of SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and SEQ ID NO: 10, wherein the set is used in nucleic acid hybridization or amplification to detect all representatives of *Salmonella enterica* subsp. *enterica, salamae, arizonae, diarizonae, houtenae, bongori* and *indica*.
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> 29. The set of isolated nucleic acid molecules of claim 22, wherein the set further comprises one or more isolated nucleic acid molecules with a length from 10 to 250 nucleotides comprising at least 10 contiguous nucleotides of a nucleic acid molecule[s] selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4 and SEQ ID NO: 5 and the complementary sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4 and SEQ ID NO: 5.
>
> 30. The set of isolated nucleic acid molecules of claim 22, wherein at least one isolated nucleic acid molecule is modified or labeled with a group selected of the group consisting of a radioactive group, a colored group, a fluorescent group, a group for immobilization on a solid phase and a group allowing an indirect or direct enzyme reaction.
>
> 31. The set of isolated nucleic acid molecules of claim 29, wherein at least one isolated nucleic acid molecule is modified or labeled with a group selected of the group consisting of a radioactive group, a colored group, a fluorescent group, a group for immobilization on a solid phase and a group allowing an indirect or direct enzyme reaction.
>
> 32. The set of isolated nucleic acid molecules of claim 22, wherein the group allowing an enzyme reaction is selected from the group consisting of antibodies, antigens, enzymes, substances having an affinity for enzymes and substances having an affinity for enzyme complexes.
>
> 33. The set of isolated nucleic acid molecules of claim 29, wherein the group allowing an enzyme reaction is selected from the group

consisting of antibodies, antigens, enzymes, substances having an affinity for enzymes and substances having an affinity for enzyme complexes.

The Examiner's new matter rejection for claim 22 should be withdrawn, because the Examiner's interpretation of the claim, as presented in the Office action dated April 16, 2008, is not contested.

I understand that the Examiner maintains the written description rejection for claims 22 and 29-33 because the Examiner does not believe that the claimed limitations for the sequences that are used to detect all representatives of *Salmonella enterica* subspecies *enterica, salamae, arizonae, diarizonae, houtenae, bongori,* and *indica* would be adequate to describe the relevant distinguishing characteristics for the *Salmonella* representative subspecies. The Examiner asserted that one of ordinary skill in the art would recognize that there is "considerable variability" between the seven subspecies of *Salmonella enterica*. The Examiner said that McClelland et al. (Nature, vol. 413, 2001, pp. 852-56) supports the assertion that two *Salmonella* subspecies, *S. bongori* and *S. arizonae* share only 85% and 83% homology with the coding sequences of the complete *S. Typhimurium LT2* chromosome.

I understand the Examiner believes that in light of this variability, the specification has not taught or provided the specific sequences that could be used to detect the different Salmonella species recited in the claims. In addition, the Examiner appears to believe that it would not be possible for one of ordinary skill in the art to determine the newly claimed sequences to detect all representatives of recited *Salmonella enterica* subspecies without an alignment of the chromosomes of the different Salmonella species.

I do not agree with the Examiner's belief about the state of the art. In my opinion, one of ordinary skill in the art would know how to align sequences and compare different strains of *Salmonella* compared to SEQ ID NO: 1 in Holmes to determine the appropriate sequence to choose from the claims. For example, textbooks like " Molecular Cloning: A Laboratory Manual" by J. Sambrook, E.F. Fritsch, and T. Maniatis, Cold Spring Harbor Laboratory Press; 2nd edition (December 1989) contain ample and detailed information in this respect. One of ordinary skill, therefore, would be able to practice the claimed invention without an alignment of the chromosomes of the different *Salmonella* species. For instance, Holmes disclosed a method to detect some *Salmonella* species by identifying a lengthy DNA nucleotide sequence and specific sequences within that DNA sequence.

Additionally, a skilled artisan knows that specific detection of food-borne pathogens by nucleic acid-based processes requires that the structure of a oligonucleotide employed for detection purposes needs to be complementary to that of the pathogen. It is further known in the art that an oligonucleotide does not need to be 100% complementary to a sequence to specifically bind to said sequence. That is to say, also oligonucleotides that are varied with respect to a particular target sequence allow for specific detection of the target sequence as long as the oligonucleotide does not hybridize to sequences different from the target sequence, e.g. a sequence from another microbial species. Given this, one of ordinary skill in the art would recognize that an oligonucleotide only needs to contain a stretch of nucleic acids that ensures hybridization to a specific target sequence.

Having regard to the instant invention, detection specificity for all the representatives of the 7 *Salmonella* subspecies is achieved by a set comprising at least 5 isolated nucleic acid molecules chosen from SEQ ID NOS: 6 to 10. However, additional nucleic acid molecules can be present. As regards the additional nucleic acid molecules, detection specificity is further on achieved if each of said additional nucleic acid molecules comprises at least a particular number of successive nucleotides matching one of SEQ ID NOS: 1 to 5. This is, because the particular number of successive nucleotides matching one of SEQ ID NOS: 1 to 5sequence is sufficient to ensure that only hybrid double-stranded nucleic acids with respect to the particular *Salmonella* target sequences are formed. One of ordinary skill, therefore, can successfully work the claimed invention without undue experimentation. In fact, it is my belief that a skilled artisan would recognize that the required detection specificity can be achieved with the instantly claimed combinations of sequences.

The parent application, which issued as U.S. Patent No. 6,706,472 ("the '472 patent"), identified ten sequences and their complements derived from an analysis of SEQ ID NO: 1 in Holmes that demonstrated the feasibility to identify all subspecies of *Salmonella enterica* with certain nucleotide sequences. Contrary to what the Examiner suggests from McClelland, the inventors of the '472 patent—the same inventors as the '731 application—demonstrated it was possible to detect the presence or absence of *Salmonella enterica* from these ten claimed sequences and their complements, thereby identifying all 37 *Salmonella enterica* strains

The present application identifies the same set of ten sequences in the '472 patent. The '731 application provides new sets of isolated nucleic acid molecules derived from the ten

sequences that may be used to detect all representatives of *Salmonella enterica* by selectively combining elements of the ten sequences and creating new nucleotide molecules that were not claimed in the '472 patent and are distinct from the prior art.

As is evident from the nucleotide sequences and claims, Holmes, the '472 patent, and the '731 application claim different nucleotide sequences, different methods for detecting *Salmonella enterica* subspecies, and different uses for the methods with regard to detecting *Salmonella enterica*, including kits for their use. As a result, the '731 application is patentably distinct yet understandable to practice for one of ordinary skill in the art.

For these reasons, it is my opinion that the Examiner's remaining rejections should be withdrawn for all of the pending claims in the '731 application.

The undersigned further declares that all statements made herein of her own knowledge are true and that all statements made on information and belief are believed to be true; and that the foregoing statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 26.08.2008 By: _____

Kornelia Berghof-Jaeger, Ph.D.